



Arrhythmias and Clinical EP

THE ROLE OF GENETICS IN VENTRICULAR TACHYARRHYTHMIA RISK STRATIFICATION: PRIMARY RESULTS FROM THE DISCOVERY TRIAL

Moderated Poster Contributions

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Authors: Heinrich Wieneke, Domenico Corrado, Jeff Lande, Javier Garcia Fernandez, Jesper Svendsen, Herve Le Marec, Juan Gabriel Martinez, Sebastian Spencker, Bernhard Strohmer, Lauri Toivonen, Winfried Siffert, St. Marien-Hospital Mülheim, Mülheim, Germany

Background: Population-based studies suggest that genetic factors contribute to sudden cardiac death (SCD), but few genetic loci have been identified. DISCOVERY investigated if 7 single nucleotide polymorphisms (SNPs) in 3 genes coding G-protein subunits were predictive for ventricular tachyarrhythmias (VT) in patients with increased SCD risk.

Methods: DISCOVERY is a prospective, international multi-center study of patients receiving an ICD for primary prevention of SCD along current guidelines. We genotyped 7 SNPs in 3 genes - GNB3 (C825T), GNAQ (GC909/908TT, G382A, G387A) and GNAS (C393T, C2273T, T2291C). There were 1145 genotyped patients with device interrogation available. Patients were followed for a median of 575 days and all VT episodes (≥ 150 bpm) were adjudicated by a physician panel blinded to genotypes. Cox regression models were used to determine if SNPs predicted time to first VT.

Results: In 297 patients, VTs occurred after ICD implant. In univariate analysis, genotypes of 2 SNPs in the GNAS gene were significantly predictive of VT (TT versus CC/CT in C393T: HR 1.42, $p=0.005$; TT versus CC/CT in C2273T: HR 1.57, $p=0.002$). Increased risk remained significant after adjustment for non-genetic covariates. TT genotype in either SNP was associated with a HR of 1.58 ($p=0.0001$, figure).

Conclusion: Genotyping may improve risk stratification for ventricular arrhythmias. Further research could reveal if GNAS SNPs can identify ventricular arrhythmia risk outside of current ICD indications.

